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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

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☐ *Additional inventors are being named on the _____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

MICROCAPSULES LOADED WITH ACTIVE INGREDIENTS AND A METHOD FOR THEIR PREPARATION

07/31/03 00491295

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ENCLOSED APPLICATION PARTS (check all that apply)

☑ Specification *Number of Pages* 36
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☐ Application Data Sheet. See 37 CFR 1.76
☐ CD(s), Number
☑ Other (specify) transmittal letter, postcard

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☑ Applicant claims small entity status. See 37 CFR 1.27.
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Date 31 July 2003

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USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C. 20231.

MAIL STOP PROVISIONAL PATENT APPLICATION
Attorney Docket No. 25616

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

NAIGERTSIK et al.

Serial No. NOT YET ASSIGNED

Filed: July 31, 2003

For: **MICROCAPSULES LOADED WITH ACTIVE INGREDIENTS AND A METHOD FOR THEIR PREPARATION**

TRANSMITTAL LETTER

Commissioner for Patents
Mail Stop Provisional Patent Application
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Alexandria, VA 22313-1450

Sir:

Submitted herewith for filing in the U.S. Patent and Trademark Office is the following **PROVISIONAL APPLICATION:**

(1) Transmittal Letter
(2) Cover sheet for filing **Provisional Application**
(3) 36 page Provisional Application consisting of:
    36 pages Textual Specification,
    0 pages of Claims,
    0 sheets of Drawings;
(4) Check No. 1956 $ 80.00 for filing fee as a small entity;
(5) Postcard for early notification of serial number.

The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account No. 14-0112.

Respectfully submitted,
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MICROCAPSULES LOADED WITH ACTIVE INGREDIENTS AND A METHOD FOR THEIR PREPARATION

FIELD OF THE INVENTION

The present invention generally relates to a composition comprising microcapsules capable of high loading of an active ingredient and to a method for their preparation. The present invention further relates to emulsions.

BACKGROUND OF THE INVENTION

Isolating functional molecules or substances in inert matrices has many useful benefits and applications where chemical contact between the active ingredient and the immediate environment should be minimized. For example, make-up compositions, such as make-up colors are currently using a very limited number of approved natural pigments and even fewer artificial organic colors. Many dyes and pigments with desired color shades of natural or synthetic origin are not approved for skin contact because their safety for direct skin contact has not been demonstrated. Isolating the colorants in transparent and inert isolating material provides a way to prevent the direct contact between the color molecules and the skin, while retaining (or even enhancing) the color intensity. Another very important application is in sunscreen compositions. The active ingredients in sunscreens have been reported to cause contact dermatitis and may cause photo contact dermatitis. Moreover, the light-excited species of these reagents may undergo photodecomposition reactions resulting in the production of free radicals and reactive oxygen species, which may bear deleterious effects on live tissues. Thus, encapsulating sunscreen active ingredients by enveloping them within a transparent silica shell offers a sophisticated way to benefit from the light-absorbing capability of sunscreens, while substantially isolating them and/or their possible photodecomposition products from the live tissues. Another example, from a totally different field, is the encapsulating of food colors either for prolonging the shelf life of food

products containing unstable natural colors such as lycopene and carotene or for isolating artificial food colors that have undesirable side effects. Encapsulating food colors of the second type in inert transparent microcapsules provides a way to prevent the digestion of these colorants while maintaining their desired color effect.

US patent Nos. 6,303,149, 6,238,650, 6,468,509, 6,436,375 and International publication Nos. WO 01/80823, WO 03/034979 and WO 03/039510 (the disclosures of these patents and publications are incorporated herein by reference in their entirety), disclose sol-gel microcapsules and methods for their preparation. In these patents and publications the loading of the active ingredients (termed also "functional molecules") is up to 95% (w/w).

US patent No. 6,365,642 discloses a process for obtaining open-celled foams by polymerizing a high internal phase (water-in-oil) emulsion, which has small amount of a continuous oil phase and a relatively greater amount of discontinuous phase. The water-in-oil emulsion taught cannot be used to form sol-gel microcapsules since the oil constitutes the external phase.

There is a widely recognized need and it will be highly advantageous to have a composition comprising a high loading (above 95% w/w) of the active ingredient and yet which is capable of minimizing the contact between the active ingredient and the environment. Such high loading is required, for example, in order to obtain high Sun Protection Factor (SPF) values, or in many other applications where high loading of an encapsulated active ingredient in the composition is required.

Additionally it will be highly advantageous to have an efficient encapsulation method which is simplified in production lower in cost (i.e less monomer and waste) and which is capable of loading high concentrations (above 95% w/w) of the active ingredient and yet preventing the leaching of the active ingredient from the microcapsules. Such a method will facilitate the encapsulation of a wide variety of molecules or substances, where the

application may demand high loading of the encapsulated molecules or substances.

Moreover, it will be highly advantageous to have an oil-in-water emulsion having a high concentration (above 50%) of the internal oily phase.

DEFINITIONS

In the present invention, the term **"active ingredient"** refers to any molecule or substance that can be used in agriculture, industry (including food industry), medicine, cosmetics, and which grants the final product (cosmetics, pesticide, drug, etc.) at least one desired property.

In the present invention, the term **"topical application"** refers to an application on the skin, hair, ears, mucous membranes, rectal application, nasal application, as well as dental application within the oral cavity.

In the present invention, the term **"TEOS"** refers to tetraethoxy silane, which is a precursor of silica.

In the present invention, the term **"loading"** refers to the weight percentage of the acive ingredient based on the total weight of the microcapsule defined by (w/w).

In the present invention, the term **"loading above 95%"** refers to a weight percentage of the acive ingredient above 95% (w/w) based on the total weight of the microcapsule.

In the present invention, the term **"sol-gel precursor"** refers to any metal or semi-metal organo-metallic monomer which allows to obtain a glass or ceramic material by the inorganic sol-gel polymerization process.

In the present invention the term **"reaction temperature"** refers to a temperature in the range 5^0C to 80^0C, preferably in the range 15^0C to 40^0C, more preferably between 18^0C and 30^0C.

SUMMARY OF THE INVENTION

According to one aspect of the present invention there is provided a composition comprising a plurality of microcapsules having a core-shell structure, wherein the core includes at least one active ingredient, the core is encapsulated within a microcapsular shell comprised of at least one inorganic polymer obtained by a sol-gel process, wherein the loading of the active ingredient within the microcapsules is above 95% w/w.

According to another aspect of the present invention there is provided a process for preparing sol-gel microcapsules loaded with above 95% (w/w) of an active ingredient, comprising the following steps;

(a) preparing an oil-in-water (o/w) emulsion by emulsification of an oily (hydrophobic) phase comprising a water insoluble sol-gel precursor and the active ingredient, in an aqueous phase comprising an aqueous solution having a pH in the range 2-7, under appropriate shear forces and temperature regime; and

(b) optionally mixing (diluting) and stirring said emulsion with an aqueous solution at a suitably selected pH in the range of 2-7, temperature and atmosphere to obtain loaded sol-gel microcapsules in a suspension;

the process comprising at least one of the following conditions:

(i) the concentration of the oily phase defined in step (a) based on the total weight of the emulsion is from 50% to 90% w/w;

(ii) the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 25/75;

(iii) the pH of the aqueous solution of step (b) is in the range 2-7, preferably in the range 2-5, more preferably in the range 3-4;

(iv) a combination of at least two of the above conditions (i), (ii) or (iii).

According to a preferred embodiment of the present invention the pH of the aqueous phase of step (a) is in the range 2-5, when both steps (a) and (b) are used in the process.

Additionally according to a preferred embodiment of the present invention the pH of the aqueous phase in step (a) is in the range 3-4, when both steps (a) and (b) are used in the process.

Moreover, according to a preferred embodiment of the present invention the pH of the aqueous phase in step (a) is in the range 3-5, when only step (a) is used in the process.

According to yet another aspect of the present invention there is provided a process for preparing sol-gel microcapsules loaded with above 95% (w/w) of an active ingredient, comprising the following steps;

(a) preparing an oil-in-water (o/w) emulsion by emulsification of an oily (hydrophobic) phase comprising a water insoluble sol-gel precursors and the active ingredient, in an aqueous phase comprising an aqueous solution having a pH in the range 2-7, under appropriate shear forces and temperature regime; and

(b) optionally mixing (diluting) and stirring said emulsion with an aqueous solution at a suitably selected pH, temperature and atmosphere to obtain loaded sol-gel microcapsules in a suspension;

the process comprising the following conditions:

(i) the concentration of the oily phase defined in step (a) based on the total weight of the emulsion is from 50% to 90% w/w;

(ii) the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 25/75; and

(iii) the pH of the aqueous solution of step (b) is in the range 2-7, preferably in the range 2 – 5, more preferably in the range 3-4.

According to a preferred embodiment of the present invention the pH of the aqueous phase of step (a) is in the range 2-5, when both steps (a) and (b) are used in the process.

Additionally according to a preferred embodiment of the present invention the pH of the aqueous phase in step (a) is in the range 3-4, when both steps (a) and (b) are used in the process.

Moreover, according to a preferred embodiment of the present invention the pH of the aqueous phase in step (a) is in the range 3-5, when only step (a) is used in the process.

According to an additional aspect of the present invention there is provided an oil-in-water emulsion comprising:

(a) an oily phase;

(b) an aqueous phase; and

(c) a surfactant

the emulsion is characterized in that the concentration of the oily phase in the emulsion is from 50% to 90% (w/w).

The surfactant may be a cationic surfactant, an anionic surfactant, a non-ionic surfactant or mixtures thereof.

According to a preferred embodiment of the present invention the surfactant is a cationic surfactant.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a composition comprising a plurality of microcapsules having a core-shell structure, wherein the core includes at least one active ingredient, the core is encapsulated within a microcapsular shell

comprised of at least one inorganic polymer obtained by a sol-gel process, wherein the loading of the active ingredient within the microcapsules is above 95% w/w.

Preferably the loading of the active ingredient within the microcapsules is from 95% to 99% w/w, more preferably the loading of the active ingredient within the microcapsules is from 95% to 98% w/w.

The composition may be useful for cosmetic or medical applications. The composition may also be used in agricultural, polymeric or food industry.

The composition may be useful for any application wherein the active ingredient should be isolated, temporaly or permanently from the ambient surroundings.

The loaded active ingredient may be any molecules or substances that are soluble or that can be suspended in the sol-gel precursor (metal or the semi metal alkoxides) of choice.

The active ingredient may be for example suncscreen agents, dental agents, fragrances, perfume, colors and dyes, food colors and food additives, waxes, antioxidants, humidifiers, vitamins, explosives, pesticides such as insecticides, herbicides and fungicides, or biological molecules such as enzymes, co-enzymes or antibodies, as well as various drugs, catalysts and reagents.

The drugs may be for example dermatological agents, anti-inflammatory agents, analgesics, anti-fungal agents, anti-biotics, anti-viral agents, anti-acne agents, anti histamines, skin whitening agents, anti-parasitic agents, muscle relaxants, steroids, hormones, astringents or mixtures thereof.

Preferably the active ingredient is a sunscreen agent.

The sunscreen agent (ultra-violet absorbing molecules or ultra-violet reflecting substances) may be for example octylmethoxy cinnamate, 3-butylmethoxydibenzoyl methane, benzophenone-3, 2-ethylhexyl p-methoxycinnamate, p-aminobenzoic acid, 2-ethylhexyl N, N-dimethyl-p-aminobenzoate, 2-cyano-3, 3-diphenylacrylic acid 2-ethylhexyl ester (octocrylene), oxybenzone, 2-phenylbenzimidizole-5-sulfonic acid, homomenthyl salicylate, octyl salycilate, 4,4'-methoxy-t-butyldibenzoylmethane, 4-isopropyl dibenzoylmethane, 3-(4-methylbenzyledene) camphor, 3-benzylidene camphor, triethanolamine salicylate, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 2,4-dihydroxybenzophenone, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 4-hydroxydibenzoylmethane, 4-N,N-(2-ethylhexyl)methyl- aminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)- benzophenone, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 4-(2-hydroxyethoxy)dibenzoylmethane or a mixture thereof.

Most preferably the sunscreen agent is octylmethoxy cinnamate, 3-butylmethoxydibenzoyl methane, benzophenone-3 or mixtures thereof.

Additional sunscreen agents which may be used in the present invention are disclosed in US patent Nos. 6,238,650, 6,468,509, 6,303,149, US 6,436,375 and International publication WO 03/039510. The disclosures of these patents and publications are incorporated herein by reference in their entirety.

The active ingredient may be for example natural food colors or synthetic food colors or food additives used in food products or oral drugs.

The active ingredient may be for example natural food colors or synthetic food colors used in cosmetic colors and skin applications.

The active ingredient may be for example pesticides such as insecticides, herbicides or fungicides used in agriculture or industry.

Preferably the inorganic polymer is prepared from a sol-gel precursor by the sol-gel process.

The sol-gel precursors may be a metal or semi-metal alkoxide monomers, or a partially hydrolyzed and partially condensed polymer thereof, or a mixture thereof.

Preferably the polymerization process is preformed through condensation-polymerization of at least one monomer (being the sol-gel precursor) selected from metal alkoxides, semi-metal alkoxides, metal esters, semi-metal esters and from monomers of the formula $M(R)_n(P)_m$, wherein M is a metallic or semi metallic element (for example Si, Ti, Zr, Al, Zn), R is a hydrolysable substituent, n is an integer from 2 to 6, P is a non polymerizable substituent and m is and integer from 0 to 6.

Alternatively, the sol-gel precursor may be an oligomer of the precursor for example, a prehydrolyzed TEOS which is based on the hydrolysis of TEOS, which may be used in order to obtain short chain polymers that can also be used for encapsulation.

In a preferred embodiment of this invention, the sol-gel precursors are silicon alkoxide monomers, or silicon ester monomers, or monomers of the formula $Si(R)_n(P)_m$, where R is a hydrolysable substituent, n is an integer from 2 to 4, P is a non polymerizable substituent and m is and integer from 0 to 4, or partially hydrolyzed and partially condensed polymer thereof, or any mixture thereof.

In another preferred embodiment of this invention, several sol-gel precursors are used together in the oil phase as a mixture of several metals or semi metal monomers, to afford a microcapsule shell which is a composite including different metal and/or semi metal elements in the final product.

The sol-gel precursors which may be used in the present invention are described in US patent Nos. 6,303,149, 6,238,650, 6,468,509, 6,436,375 and International publication Nos. WO 01/80823, WO 03/034979 and WO 03/039510 (the disclosures of these patents and publications are incorporated herein by reference in their entirety).

Recognizing that metal and semi metal alkoxide monomers (and their partially hydrolyzed and condensed polymers) such as tetramethoxy silane (TMOS), tetraethoxy silane (TEOS), methyl tetraethoxy silane (MeTEOS) *etc.* are very good solvents for numerous molecules and substances is highly advantageous since it facilitated the utilization of this solubility property to load the dissolved molecules or substances in the hydrolysis-condensation polymer of the monomer solvent. Nonetheless, the present invention may also be used to coat or load particles or substances which can be suspended in the sol-gel precursors.

Preferably the sol-gel precursor is a silicon alkoxide monomer such as tetramethoxy silane (TMOS), tetraethoxy silane (TEOS), methyl triethoxy silane (MeTEOS).

Preferably the active ingredient is a sunscreen agent and the sol-gel precursor is tetraethoxy silane (TEOS).

The microcapsules of the present invention may be useful for human or non-human applications, as they may be easily incorporated in various carriers. The microcapsules may be easily dispersed or suspended in a carrier or diluent.

Simple mixing with any suitable mixer or stirrer is sufficient to achieve an effective dispersion. If necessary high shear forces may be applied to facilitate fast and efficient mixing of the microcapsules in the carrier.

The carrier may be for example a pharmaceutical carrier, a cosmetic carrier, a food carrier or any other carrier used in agriculture or industry.

The carrier may be a liquid, a semi solid or a solid carrier.

The carrier may be for example an emulsion, a cream, an aqueous solution, an oil, an ointment, a paste, a gel, a lotion, a milk, a suspension, a powder, a processed food , a spray, a paint, a lacquer, a coating, a plastic or a detergent.

The carrier may further comprise at least one non-encapsulated active ingredient.

The final form of the composition may be for example an emulsion, an aqueous solution, an oil, a semi-solid formulation (such as a cream, an ointment, a paste, or a gel), a lotion, a milk, a suspension, a powder, a capsule, an aerosol, a spray, a foam, a shampoo, a hair conditioner, a lacquer, a makeup, a solid stick, a toothpaste, a food, a paint, a plastic or a coating.

The particle size of the microcapsules can be controlled to the range 0.01-1000μm, preferably 0.1-100μm, more preferably 1-10μm in diameter.

The composition may be in the form of a suspension or a powder wherein the powder particles or the suspended particles are of 0.01 - 1000μ in diameter.

The compositions of the present invention may be applied topically.

The composition may be in the form of a suspension or a powder wherein the powder or the suspension includes 0.1-10μ (diameter) spherical particles, has a smooth texture, and is transparent when suspended in cosmetic or skin care formulations and applied to skin.

By one embodiment the microcapsules of the present invention are leachless, this is highly advantageous since encapsulation of a sensitive active ingredient in the sol-gel microcapsules can protect it from other ingredients in the formulation and from the environment, and thus extends the shelf life of the end-product. The active ingredients in sunscreens have been reported to cause contact dermatitis and may cause photo contact dermatitis. Moreover, the light-excited species of these reagents may undergo photodecomposition reactions resulting in the production of free radicals and reactive oxygen species, which may bear deleterious effects on live tissues. Therefore, formulating leachless microcapsules is particularly advantageous in sunscreen compositions where there is a need to isolate the sunscreen active agents an/or their possible photodecomposition products from the live tissues.

Additional examples and applications in which isolation of the active ingredients from the environment is advantageous are described in the background of the invention.

By another embodiment the microcapsules of the present invention are designed to release the active ingredient.

In certain applications such as medical (oral or topical) or agricultural it may be desired to achieve immediate or controlled release of the active ingredient from the microcapsules.

The release of active ingredient from the microcapsule can be designed to be immediate, delayed or sustained; this can be controlled by varying the composition of the microcapsular shell, its diameter, and by varying the composition of the carrier surrounding the microcapsules.

Release can be obtained and controlled by aging time, thermal treatment or any mechanical mean that can change the characteristic porosity or strength of the shell, or chemical mean like organic polymers and/or surfactants that may be added while the sol-gel microcapsules are being formed, to control the surface nature of the shell and the rate of diffusion through the pores. Since the microcapsular shell may be composed of sub-micron particles, the effective pore size of the shell may be controlled by electrolytes or any other chemical component of the formulation. This may be a trigger for release of the active ingredients from the microcapsules.

Since the encapsulation creates micro-domains within the entire formulation, one active ingredient can be encapsulated while a second active ingredient can be present in the carrier that surrounds the microcapsules. This is advantageous when the ingredients acts synergistically together, yet one is chemically reactive with another.

Alternatively each of the active ingredients may be microencapsulated in separate sol-gel microcapsules.

In an alternative, the active ingredient may be encapsulated alone, or with other ingredients within the same microcapsule. Co-encapsulation of compounds that enhance stability of the sensitive ingredient is beneficial. For example, anti oxidants can be co-encapsulated with oxygen-sensitive or oxidant-sensitive ingredients, to give "localized protection".

The present invention additionally relates to a process for the preparation of sol-gel microcapsules, loaded with above 95% of an active ingredient.

The sol-gel particles encase or encapsulate (hereinafter called loading) the active ingredient.

The sol-gel microcapsules may be in the range of 0.01-1000μ, preferably 0.1-100μ, more preferably 1-10μ, in diameter.

The process is based on the preparation of an oil-in-water emulsion by emulsifying a hydrophobic solution that comprises the sol-gel precursors and the molecules or substances to be loaded, in aqueous solution, with or without the need for mixing said emulsion with another aqueous solution to accelerate the condensation-polymerization reaction.

In the present invention the term "mixing" also relates to dropwise addition of one solution to the other, by pouring one solution to the other, or any other method of combining the two solutions together.

Surprisingly it was found in the present invention that decreasing the weight ratio of the sol-gel precursor to the active ingredient to the range of 5/95 – 25/75, preparing a concentrated oil-in water emulsion wherein the concentration of the oily phase in the emulsion is above 50% (w/w), and performing the condensation-polymerization process in a pH of 2-7, preferably 2-5, and more preferably 3-4, enables an efficient encapsulation of the active ingredient with high loading (above 95%) of the active ingredient and yet prevents the leaching of the active ingredient from the microcapsules.

Unexpectedly it was found that although the weight ratio of the sol-gel presursor to the active ingredient was decreased from the prior art typical data of about 50/50 to the range of 5/95 – 25/75, the polymerization of the sol-gel precursor was of high efficiency and a higher yield was obtained from the point of view of the quantity of silica developed on the shell of the microcapsule, as revealed by the high loading of the active ingredient and insignificant amount of the residual sol-gel precursor in the reaction aqueous medium in which the microcapsules are produced. This is highly advantageous since it minimizes the environmental contamination, does not require treatment of the reaction waste water and thus simplifies and lowers the cost of the process.

Another advantage of the process of the present invention is the elimination of the step of isolation of the microcapsules by centrifugation,

filtration, re-suspension etc, which is needed in the prior art in order to obtain a high concentration of particles in the final product (in previous patent we needed to isolate the microcapsules from the mother liquor in order to obtain a concentration of 40% (by weight) of sunscreen in the suspension, while in the present invention we obtain it at the and of the reaction due to the high loading of the active ingredient in the oil phase at the emulsion step).

Performing the condensation-polymerization process in a pH range of 2-7, preferably in the range of 2-5, and more preferably in the range of 3-4 was found to be highly advantageous since at this catalytic pH a more linear polycondensation reaction is obtained at the oil-water interface of the emulsion, thereby reducing the risk of coalescence between the oil drops which can take place at a higher pH. At a higher pH (above pH 7) a random fast polycondensation reaction produces lots of oligomers which promotes the interconnection of the dispersed oil drops.

Surprisingly it was found in the present invention, in accordance to the leachless aspect, that the leaching of the microcapsules loaded with an active ingredient, being the sunscreen agent, into cosmetic oils or into an aqueous solution including a surfactant is less than 1%, preferably less than 0.5% after vigorous shaking.

The present invention additionally relates to a process for preparing sol-gel microcapsules loaded with above 95% (w/w) of an active ingredient, comprising the following steps;

(a) preparing an oil-in-water (o/w) emulsion by emulsification of an oily (hydrophobic) phase comprising a water insoluble sol-gel precursor and the active ingredient, in an aqueous phase comprising an aqueous solution having a pH in the range 2-7, under appropriate shear forces and temperature regime; and

(b) optionally mixing (diluting) and stirring said emulsion with an aqueous solution at a suitably selected pH in the range 2-7, temperature and atmosphere to obtain loaded sol-gel microcapsules in a suspension;

the process comprising at least one of the following conditions:

(i) the concentration of the oily phase defined in step (a) based on the total weight of the emulsion is from 50% to 90% w/w;

(ii) the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 25/75;

(iii) the pH of the aqueous solution of step (b) is in the range 2-7, preferably in the range 2 – 5, more preferably in the range 3-4;

(iv) a combination of at least two of the above conditions (i), (ii) or (iii).

The present invention further relates to process for preparing sol-gel microcapsules loaded with above 95% (w/w) of an active ingredient, comprising the following steps;

(a) preparing an oil-in-water (o/w) emulsion by emulsification of an oily (hydrophobic) phase comprising a water insoluble sol-gel precursors and the active ingredient, in an aqueous phase comprising an aqueous solution having a pH in the range 2-7, under appropriate shear forces and temperature regime; and

(b) optionally mixing (diluting) and stirring said emulsion with an aqueous solution at a suitably selected pH, temperature and atmosphere to obtain loaded sol-gel microcapsules in a suspension;

the process comprising the following conditions:

(i) the concentration of the oily phase defined in step (a) based on the total weight of the emulsion is from 50% to 90% w/w;

(ii) the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 25/75; and

(iii) the pH of the aqueous solution of step (b) is in the range 2-7, preferably in the range 2 – 5, more preferably in the range 3 - 4.

In all processes described in the present invention:

Preferably the loading of the active ingredient within the microcapsules is from 95% to 99% w/w, more preferably the loading of the active ingredient within the microcapsules is from 95% to 98% w/w.

The concentration of the oily phase in the emulsion of step (a) may be from 50% to 80% (w/w).

The concentration of the oily phase in the emulsion of step (a) may be from 50% to 70% (w/w).

The concentration of the oily phase in the emulsion of step (a) may be from 55% to 70% (w/w).

The concentration of the oily phase in the emulsion of step (a) may be from 60% to 70% (w/w).

The concentration of the oily phase in the emulsion of step (a) may be from 65% to 70% (w/w).

When both steps (a) and (b) are used in the process, the pH of the aqueous phase of step (a) is preferably in the range 2-5, and more preferably the pH of the aqueous phase in step (a) is in the range 3-4.

When only step (a) is used in the process, the pH of the aqueous phase of step (a) is preferably in the range 3-5.

Preferably the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 20/80.

More preferably the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 5/95 to 15/85.

Most preferably the weight ratio of the sol-gel precursors defined in step (a) to the active ingredient is from 10/90 to 15/85.

All the processes of the present invention may be conducted by one step – using only step (a) (and omitting step (b)).

The polymerization of the sol-gel precursors may occur in step (a), thereby the microcapsules in suspension may be obtained at the end of step (a) without further treatment.

The emulsion is prepared at a temperature between 5- 20°C, preferably 10 –18°C. In a subsequent step the reaction may be heated to a reaction temperature above 20°C. The pH of the emulsion may be between 2-7, more preferably between pH 3-5 in order to encourage the reaction to proceed at room temperature.

According to a preferred embodiment of the present invention, the processes of the present invention are conducted by two steps (both step (a) and step (b)).

The encapsulation of the active ingredient was found to be more efficient when conducting the process by both steps (a) and (b) compared to one step (only step (a)) process.

The oily phase comprising the sol-gel precursor and the active ingredient is water immisible.

The emulsion obtained in step (a) and/or the mixture of step (b) may further include an additional step selected from the group consisting of: heating, cooling, subjecting to vacuum or pressure, keeping under inert gas

atmosphere, subjecting to changes in pH and subjecting to an aging period preferably of up to 14 days.

In the present invention, the term "aging" refers to the period of time added over the end of the microcapsular shell (silica-shell) formation, needed in order to obtain the smallest leaching rate of the active due to closure of the open pores of the shell.

The hydrophobic oily phase in step (a) and/or the aqueous solution in steps (a) and/or (b) may include additional surfactants or any additives to improve the product.

The surfactant may be for example an anionic surfactant, a cationic surfactant, a non-ionic surfactant, an anionic polymeric surfactant, a cationic polymeric surfactant, a non-ionic polymeric surfactant, or mixtures thereof.

The emulsification in step (a) is performed using at least one emulsification agent (surfactant).

The aqueous solution of step (a) may comprise at least one hydrophilic (water soluble) surfactant.

The oily phase of step (a) may comprise at least one hydrophobic surfactant.

The oily phase of step (a) may comprise at least one hydrophobic polymeric surfactant.

Preferably hydrophobic surfactant or hydrophobic polymeric surfactant is a non-ionic surfactant.

The hydrophilic surfactant may be for example an anionic, a cationic, an non-ionic surfactant or mixtures thereof.

The emulsification in step (a) is preferably performed using at least one hydrophilic surfactant.

Peferably the hydrophilic surfactant is a cationic surfactant.

Most preferably the cationic surfactant is cetyltrimethyl ammonium chloride.

Additional surfactants which may be used in the present invention are described in: Cationic Surfactants, edited by Eric Jungermann from the series Surfactant Science series volume 4, see also volumes 34, 37, 53 of the same series, incorporated herein by reference in their entirety; and Remington's Pharmaceutical Sciences, 16th ed., Mack Publishing Company, Easton, Pennsylvania. (1980), incorporated herein by reference in its entirety.

The concentration of the cationic surfactant in the aqueous solution (aqueous phase) may be from 0.1 to 5% (w/w) and most preferably from 0.5 to 1.5 (w/w).

Surprisingly it was found in the present invention that the cationic surfactant, cetyltrimethyl amoniumchloride, used as a single emulsifying agent at low concentrations is capable of emulsifying a concentrated oil-in-water emulsion comprising above 50% w/w of the oily phase based on the total weight of the emulsion. The emulsion formed was found to be stable for at least 3 – 4 hours at room temperature.

The process optionally comprises an additional step of isolating and rinsing the microcapsules through cycles of separation by centrifuge or by filtration and re-suspension in water, or by evaporation and re-suspension in water or by dialysis or by any other conventional means known in the art.

The suspension so obtained may be stabilized by adding additives such as non-ionic, cationic or anionic polymers, or any other suitable suspending agent to obtain the final product in a suspension form.

The process may further comprise the step of removing the water by any conventional means to obtain the final product in a powder form.

The process may further comprise the step of adding-reconstitution additives such as non-ionic, cationic or anionic surfactants or polymers.

The sol-gel precursors may be a metal or a semi-metal alkoxide monomers, or a partially hydrolyzed and partially condensed polymer thereof, or a mixture thereof.

The polymerization progresses is preformed through condensation-polymerization of at least one monomer (sol-gel precursor) selected from metal alkoxides, semi-metal alkoxides, metal esters, semi-metal esters and from monomers of the formula $M(R)_n(P)_m$, wherein M is a metallic or semi metallic element (for example Si, Ti, Zr, Al, Zn), R is a hydrolysable substituent, n is an integer from 2 to 6, P is a non polymerizable substituent and m is an integer from 0 to 6.

Alternatively, the sol-gel precursor may be an oligomer of the precursor for example, a prehydrolyzed TEOS which is based on the hydrolysis of TEOS, which may be used in order to obtain short chain polymers that can also be used for encapsulation.

In a preferred embodiment of this invention, the sol-gel precursors are silicon alkoxide monomers, or silicon ester monomers, or monomers of the formula $Si(R)_n(P)_m$, where R is a hydrolysable substituent, n is an integer

from 2 to 4, P is a non polymerizable substituent and m is an integer from 0 to 4, or partially hydrolyzed and partially condensed polymer thereof, or any mixture thereof.

In another preferred embodiment of this invention, several sol-gel precursors are used together in the oil phase as a mixture of several metals or semi metal monomers, to afford a microcapsule shell which is a composite including different metal and/or semi metal elements in the final product.

The sol-gel precursors which may be used in the present invention are described in US patent Nos. 6,303,149, 6,238,650, 6,468,509, 6,436,375 and International publication Nos. WO 01/80823, WO 03/034979 and WO 03/039510 (the disclosures of these patents and publications are incorporated herein by reference in their entirety).

Recognizing that metal and semi metal alkoxide monomers (and their partially hydrolyzed and condensed polymers) such as tetramethoxy silane (TMOS), tetraethoxy silane (TEOS), methyl tetraethoxy silane (MeTEOS) *etc.* are very good solvents for numerous molecules and substances facilitated the development of this method, which utilizes this solubility property to load the dissolved molecules or substances in the hydrolysis-condensation polymer of the monomer solvent. Nonetheless, the present invention may also be used to coat or load molecules or substances, which can be suspended in the sol-gel precursors.

The loaded active ingredient may be any molecule or substances that are soluble or that can be suspended in the sol-gel precursor (metal or in the semi metal alkoxides) of choice.

The active ingredient may be for example sunscreen agents, dental agents, fragrances, perfume, colors and dyes, food colors and food additives,

waxes, antioxidants, humidifiers, vitamins, explosives, pesticides such as insecticides, herbicides and fungicides, or biological molecules such as enzymes, co-enzymes or antibodies, as well as various drugs, catalysts and reagents.

The drugs include but not limited to dermatological agents, dental agents, anti-inflammatory agents, analgesics, anti-fungal agents, anti-biotics, anti-viral agents, anti-acne agents, anti histamines, skin whitening agents, anti-parasitic agents, muscle relaxants, steroids, hormones, astringents, or mixtures thereof.

Preferably the active ingredient is a sunscreen agent.
The sunscreen agent (ultra-violet absorbing molecules or ultra-violet reflecting substances) may be for example
octylmethoxy cinnamate, 3-butylmethoxydibenzoyl methane, benzophenone-3, 2-ethylhexyl p-methoxycinnamate, p-aminobenzoic acid, 2-ethylhexyl N, N-dimethyl-p-aminobenzoate, 2-cyano-3, 3-diphenylacrylic acid 2-ethylhexyl ester (octocrylene), oxybenzone, 2-phenylbenzimidizole-5-sulfonic acid, homomenthyl salicylate, octyl salycilate, 4,4'-methoxy-t-butyldibenzoylmethane, 4-isopropyl dibenzoylmethane, 3-(4-methylbenzyledene) camphor, 3-benzylidene camphor, triethanolamine salicylate, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 2,4-dihydroxybenzophenone, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 4-hydroxydibenzoylmethane, 4-N,N-(2-ethylhexyl)methyl- aminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)- benzophenone, 4-N,N-(2-ethylhexyl)methyl aminobenzoic acid ester of 4-(2-hydroxyethoxy)dibenzoylmethane or a mixture thereof.

Most preferably the sunscreen agent is octylmethoxy cinnamate, 3-butylmethoxydibenzoyl methane, benzophenone-3, or mixtures thereof.

Additional sunscreen agents which may be used in the present invention are disclosed in US patent Nos. 6,238,650, 6,468,509, 6,303,149, US 6,436,375 and International publication WO 03/039510. The disclosures of these patents and publications are incorporated herein by reference in their entirety.

The active ingredient may be for example natural food colors or synthetic food colors or food additives used in food products or oral drugs.

The active ingredient may be for example natural food colors or synthetic food colors used in cosmetic colors and skin applications.

The active ingredient may be for example pesticides such as insecticides, herbicides or fungicides used in agriculture or industry.

The product obtained by the process may be in a powder form or a suspension form. The powder particles or suspended particles may be in the range of 0.01 – 1000μ, preferably 0.1 – 100μ, more preferably 1 – 10 μ in diameter.

The product by process may accordingly vary for human or non-human applications, as the obtained aqueous suspension and the obtained dry powder may be easily incorporated in various carriers, such as creams and lotions, processed food, sprays, paints, lacquers, coatings, plastics and detergents.

Incorporation of the final product either in the form of a suspension or a powder in cosmetic formulations affords a transparent cream when applying to skin and has a smooth and pleasant contact.

Preferably the powder or suspension include spherical particles in the range of 0.1 – 10μ in diameter and has a smooth texture and is transparent

when suspended in cosmetic or skin care formulations and when applied to the skin.

Preferably the leaching of the loaded active ingredient from the microcapsules into cosmetic oils or into surfactant-containing aqueous solution is less than 0.5%, preferably less than 0.2%, after vigorous shaking.

The process of the present invention may further include the step of modifying the surface charge of the products by adding anionic or cationic surfactants or polymers during any step of the process.

The process of the present invention may be conducted by the following steps:

(a) A solution consisting of the water insoluble sol-gel precursors (such as metal alkoxides) with or without a co-solvent and/or surfactant and the molecules to be encapsulated is emulsified in an aqueous solution having a pH in the range of 2-7, that may contain various surfactants, i.e. cationic, anionic or non-ionic surfactants, which are utilized to assist in stabilizing the emulsions. This emulsion is created under appropriate shear forces, utilizing an apparatus such as a homogenizer, a high-pressure homogenizer, a sonicator or membranes. The oil phase of the emulsion may optionally contain additives for improving the process and/or for obtaining an improved product. Examples for such additives are viscosity modifying reagents (i.e., thickeners), acids or bases that dissolve in the sol-gel precursor of choice and assist in catalyzing the hydrolysis-condensation polymerization reaction, surfactants and others.

(b) The emulsion obtained by step (a) may be optionally mixed with an aqueous solution at a suitably selected pH (preferably a pH in the range of 2-7), which may also contain additional surfactants. The aqueous solution may also contain additives for improving the process and/or for obtaining an improved product such as water glass.

The emulsion obtained in step (a) and/or the reaction mixture of step (b) may be heated or cooled, subject to vacuum, or pressure, or kept under inert gas atmosphere, subject to changes in pH, or subject to an optional further aging period at room or accelerated temperature.

The resulting particles (microcapsules) can be optionally isolated and rinsed through cycles of centrifuge or filtration and re-suspension in deionized water or by dialysis or by any other technique known in the art.

The water insoluble solution (of step (a)) and the aqueous solutions (of steps (a) and (b) and of the optional further rinses) may contain various surfactants and any other additives for improving the process and/or the product.

Since the encapsulation process of the present invention is highly efficient, resulting in minute amounts of by products or reaction precursors such as the sol-gel precursors in the aqueous reaction mixture, the obtained suspension of step (a) or (b) may be used without further treatment (such as rinsing, centrifugation, filtration, resuspension).

Occasionally, the reaction medium of the microcapsules may be changed for example by diafiltration, addition or replacement of the reaction medium.

The obtained suspension of step (a) or (b) may be incorporated for example into a suitable carrier.

The final product may be used in a dispersion form, after re-suspension in water with optional addition of suitable additives such as non-ionic, cationic or anionic polymers, or any other suspension aid known to the skilled artisan in this field. This dispersion shows extremely low leaching of the encapsulated material into surfactants solution in water, or into cosmetic oils.

The final product may also be used in a powder form, after removal of the water by appropriate means (drying, lyophilization, etc.) with optional

addition of reconstitution additives such as non-ionic, cationic or anionic surfactants or polymers.

The loading of the loaded active ingredient molecules or substances in the sol-gel microcapsules is above 95% by weight of the solid (total weight of the microcapsule). The loading of the loaded molecules or substances in the final aqueous dispersion may be up to 75% wt/wt of the aqueous suspension.

Under appropriate choice of the reaction conditions the product is in the form of an aqueous suspension of up to 75% solids, consisting of sphere particles of 0.1-10μm in diameter or in the form of fine free-flowing powder of sphere particles of 0.01-1000μm in diameter.

By selecting the appropriate reaction conditions, the particle size of the final product can be controlled to be in the range from 0.01 to 1000μ in diameter and the leaching degree of the loaded molecule into cosmetic oils or into the surfactant-containing aqueous solution can be minimized.

The particle size (diameter) of the final product can be controlled to the range 0.01 - 1000μ, preferably 0.1-100μ, more preferably 0.1 - 10μ. The particles obtained by the present process can sustain high shear forces such as those present in a homogeizer or a sonicator without change in their encapsulation properties or in particle size distribution. The particles can also sustain increased temperatures up to 80°C for 2 hours, γ-irradiation treatment up to 50kGy without any such change.

In a preferred embodiment of the present invention, under appropriate choice of the reaction conditions, said product is in the form of a suspension containing about 1 to 75% solids consisting of sphere particles of 0.1-10μ in diameter. Said suspension may be stabilized with the aid of suitable additives such as non-ionic, cationic or anionic polymers, or any other suspension aid known to the skilled artisan in this field. This suspension shows extremely low leaching of the encapsulated material into surfactants solution in water, or into

cosmetic oils. Incorporation of this aqueous suspension in a cosmetic formulation affords a transparent cream when applying to skin and has a smooth and pleasant contact.

In another preferred embodiment of the present invention, under appropriate choice of the reaction conditions said product is in the form of a fine powder with a smooth and pleasant texture consisting of sphere particles of 0.1-10μ in diameter. Dispersion of this powder in a cosmetic formulation affords a transparent cream when applying to skin and has a smooth and pleasant contact.

The product by process may be designed to hold and/or isolate the encapsulated molecules or substances within the sol-gel microcapsules.

The present invention further relates to an oil-in-water emulsion comprising:

(a) an oily phase;

(b) an aqueous phase; and

(c) a surfactant

the emulsion is characterized in that the concentration of the oily phase in the emulsion is from 50% to 90% (w/w).

The concentration of the oily phase in the emulsion may be from 50% to 80% (w/w).

The concentration of the oily phase in the emulsion may be from 50% to 70% (w/w).

The concentration of the oily phase in the emulsion may be from 55% to 70% (w/w).

The concentration of the oily phase in the emulsion may be from 60% to 70% (w/w).

The concentration of the oily phase in the emulsion may be from 65% to 70% (w/w).

The surfactant may be an anionic surfactant, a cationic surfactant, a non-ionic surfactant or mixtures thereof.

Preferably the surfactant is a cationic surfactant.

Preferably the cationic surfactant is cetyltrimethyl ammonium chloride.

Additional surfactants which may be used in the present invention are described in: Cationic Surfactants, edited by Eric Jungermann from the series Surfactant Science series volume 4, see also volumes 34, 37, 53 of the same series, incorporated herein by reference in their entirety; and Remington's Pharmaceutical Sciences, 16th ed., Mack Publishing Company, Easton, Pennsylvania. (1980), incorporated herein by reference in its entirety.

The concentration of the cationic surfactant in the aqueous phase maybe from 0.1 to 5% (w/w) and most preferably from 0.5 to 1.5% (w/w).

The active ingredient may be as described above.

Preferably the oily phase comprises at least one active ingredient and at least one sol-gel precursor as described above.

The sol-gel precursors may be a metal or a semi-metal alkoxide monomers, or a partially hydrolyzed and partially condensed polymer thereof, or a mixture thereof.

The sol-gel precursors may be at least one monomer selected from metal alkoxides, semi-metal alkoxides, metal esters, semi-metal esters and from monomers of the formula $M(R)_n(P)_m$, wherein M is a metallic or semi metallic element (for example Si, Ti, Zr, Al, Zn), R is a hydrolysable

substituent, n is an integer from 2 to 6, P is a non polymerizable substituent and m is an integer from 0 to 6.

Alternatively, the sol-gel precursor may be an oligomer of the precursor for example, a prehydrolyzed TEOS which is based on the hydrolysis of TEOS, which may be used in order to obtain short chain polymers that can also be used for encapsulation.

In a preferred embodiment of this invention, the sol-gel precursors are silicon alkoxide monomers, or silicon ester monomers, or monomers of the formula $Si(R)_n(P)_m$, where R is a hydrolysable substituent, n is an integer from 2 to 4, P is a non polymerizable substituent and m is an integer from 0 to 4, or partially hydrolyzed and partially condensed polymer thereof, or any mixture thereof.

In another preferred embodiment of this invention, several sol-gel precursors are used together in the oil phase as a mixture of several metals or semi metal monomers, to afford a microcapsule shell which is a composite including different metal and/or semi metal elements in the final product.

The sol-gel precursors which may be used in the present invention are described in US patent Nos. 6,303,149, 6,238,650, 6,468,509, 6,436,375 and International publication Nos. WO 01/80823, WO 03/034979 and WO 03/039510 (the disclosures of these patents and publications are incorporated herein by reference in their entirety).

It should be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description. The invention includes other embodiments and can be practiced or implemented in various ways. Also, it is

to be understood that the phraseology and terminology employed herein is for the purpose of description only and should not be regarded as limiting.

EXAMPLES

The following examples clarify and demonstrate the present invention. They are not under any circumstances exclusive and do not intend to limit the scope of the present invention.

Background to examples

As was mentioned in the background, the case of encapsulated sunscreen agents is of a special importance. Sunscreen products are widely used all over the world by all ages and gender, however, not only that the active ingredients in these products may cause contact dermatitis, but also the light-excited species of these reagents may cause photo contact dermatitis. Thus, encapsulating sunscreen active ingredients in transparent sol-gel microcapsules like silica offers a sophisticated way to benefit from the light-absorbing capability of sunscreens, while substantially isolating them and/or their possible photodecomposition products from the live tissues.

EXAMPLE 1 - octylmethoxy cinnamate (OMC) in TEOS (tetraethoxy silane).

Octylmethoxy cinnamate (OMC), a widely used sunscreen has been encapsulated in sol-gel microcapsules (silica microcapsules) by the following procedure:

276g OMC was mixed with 24g TEOS. The organic phase was emulsified in 161g of aqueous solution containing 1% cetyltrimethyl ammonium chloride (CTAC) under high shear forces using a PT 6100 Polytron homogenizer at 9000rpm for 5minute. The vessel walls were cooled by immersion in an ice-water bath during the homogenizing process. This emulsion was then poured into an IKA LR-A 1000 Laboratory reactor, equipped with Eurostar Power

control-visc P4 stirrer, containing 230.5g of an aqueous solution having a pH of 3.8. The mixture was stirred at 400 rpm until the emulsion was completly mixed with the acidic solution, then the stirring rate was lowered to 60 rpm. The microcapsules obtain at the end of the reaction were isolated using a Sorvall RC-5C PLUS centrifuge equipped with SLA-1500 head at 12500RPM for 30min. The cake obtained by this process was reconstituted and stirred in pure water and further isolated by the same process. The cake obtained at the end of this process was reconstituted in an aqueous solution containing dispersants, preservatives and pH stabilizers.

The composition of the microcapsules obtained by this process consists of 97.55% (w/w) OMC, enveloped in a tiny silica shell having a particle size ranging between 0.75 and 2.5 μ.

Formulation of the microcapsule suspension obtained by this process is described in Formula A, (Example 5, Table 1) which affords a transparent smooth and pleasant cream when applied on the skin

EXAMPLE 2 - benzophenone-3 (BP-3) and OMC in TEOS

82.8g benzophenone-3, an UV-B as well as UV-A sunscreen agent, was dissolved in 193.2g OMC. The obtained mixture was dissolved in 24g TEOS and the organic phase was emulsified under high shear forces (same as described in Example 1) in 161g aqueous solution containing 1% cetyltrimethyl ammonium chloride (CTAC). The obtained emulsion was then poured into the reactor (same as above) containing 230g HCl aqueous solution at pH=3.5. The mixture was stirred at 400 rpm until the emulsion was completly mixed with the acidic solution, then the stirring rate was lowered to 60 rpm. The microcapsules obtain at the end of the reaction were isolated using a Sorvall RC-5C PLUS centrifuge equipped with SLA-1500 head at 12500RPM for 30min. The cake obtained by this process was reconstituted and

stirred in pure water and further isolated by the same process. The cake obtained at the end of this process was reconstituted in an aqueous solution containing dispersants, preservatives and pH stabilizers.

The composition of the microcapsules obtained by this process consists of 98.0 % (w/w) BP-3/OMC solution, enveloped in a tiny silica shell having a particle size ranging between 0.75 and 2.5 μ.

Formulation of this product in a neutral cosmetic cream (w/o lotion, from a commercial source) afforded a cosmetic cream with a broad absorption spectrum in the UV, as expected from a mixture of those two sunscreens used. As a result a transparent smooth and pleasant feel cream was obtained when applied on the skin.

EXAMPLE 3- butylmethoxydibenzoyl methane (BMDBM) in 2-Ethylhexyl-2-cyano-3, 3-diphenylacrylate (Octocrylene)

85.5g BMDBM, a UVA sunscreen agent, was completely dissolved in 199.5g octocrylene (UVB absorber) at 40degC for 3 hours under intensive stirring. The obtained mixture was mixed with 15g TEOS. The oil phase was then emulsified in 161g of aqueous solution containing 1% (w/w) cetyltrimethyl ammonium chloride (CTAC) under high shear forces using a PT 6100 Polytron homogenizer at 15000rpm for 10minute. The vessel walls were cooled by immersion in an ice-water bath during the homogenizing process. This emulsion was then poured into an IKA LR-A 1000 Laboratory reactor, equipped with Eurostar Power control-visc P4 stirrer, containing 230.5g HCl aqueous solution at pH 3.8. The mixture was stirred at 400 rpm until the emulsion was completly mixed with the acidic solution, then the stirring rate was lowered to 60 rpm. The microcapsules obtain at the end of the reaction were isolated using a Sorvall RC-5C PLUS centrifuge equipped with SLA-

1500 head at 12500RPM for 30min. The cake obtained by this process was reconstituted and stirred in pure water and further isolated by the same process. The cake obtained at the end of this process was reconstituted in an 1% polyvinyl pyrrolidon (PVP K30, ISP) to afford a stable dispersion. The composition of the microcapsules obtained by this process consists of BMDBM/OCT solution enveloped in a tiny silica shell having a particle size of 0.3-2.7 μ and an aqueous solution containing dispersants, preservatives and pH stabilizers

Formulation of this product in a neutral cosmetic cream (w/o lotion, from a commercial source) afforded a cosmetic cream with a broad absorption spectrum in the UV, as expected from a mixture of those two sunscreens used. As a result a transparent smooth and pleasant feel cream was obtained when applied on the skin.

EXAMPLE 4

Leaching –out test for the encapsulated OMC in water suspension:

In order to test the encapsulation properties of the microcapsules a leaching-out test was developed. It was found that vigorous shaking of the suspenson in 3% polyoxyethylene 20 sorbitan monostearate (Tween 60) solution in water at room temperature, followed by filtration of the particles (0.2μ cut off filter), and spectral analysis of the filtrate, gives a linear response at the range 0-0.2%(w/w) which reflects the concentration of free active ingredient in the surfactant solution. This surfactant solution is commonly used in cosmetic formulations. The ability of this solution to solubilize encapsulated ingredients in water was confirmed by testing this procedure on encapsulated ingredients. The leaching out rate measured as described here for particles in suspension was less than 0.3%.

No significant changes in the leaching rate under the same conditions was observed after homogenization of the suspension with an IKA product type disperser rotated at 2000RPM for 35min and after γ-irradiation treatment at 2.5Mrad.

EXAMPLE 5

In order to test the integrity of the encapsulation ability of the microcapsules after formulation in the cosmetic carrier described in table 1, a leaching-out test was developed. In this test the formulated particles are submitted to a vigorous shaking in a 3% polyoxyethylene 20 sorbitan monostearate (Tween 60) aqueous solution at room temperature followed by filtration of the particles (0.2μ cut off filter), and spectral analysis of the filtrate. The results show a linear response at the range 0-0.15%(w/w) which reflects the concentration of free active ingredient in the surfactant solution, which clearly show that the integrity of the encapsulation was saved.

Table 1: Formulation containing sunscreen-loaded particles obtained by the process of the present invention

Formulation ingredients	% in formulation
water	80.7
Squalene	5.0
Glyceryl stearate & PEG-100 stearate	5.0
Cetyl alcohol	2.0
Methyl parabene	0.1
Propyl parabene	0.1
Encapsulated OMC in final formulation	7.0
Leaching-out, %(w/w)	0.15
Leaching out rate, %/h (w/w)	0.06